```
=> His L1
MISSING OPERATOR HIS L1
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> L1
L2      383454 L1

=> L2
L3      383454 L1

=> reovirus
L4        5716 REOVIRUS

=> chemothrapy
L5          20 CHEMOTHRAPY

=> cisplatin
L6       71217 CISPLATIN

=> L4 and L6
L7           2 L4 AND L6

=> interferon
L8      253270 INTERFERON

=> L8 and L4
L9         473 L8 AND L4

=> oncolysis
L10        445 ONCOLYSIS

=> L9 and L10
L11          0 L9 AND L10

=> cancer and L9
L12          7 CANCER AND L9

=> D L12 IBIB AB 1-7

L12  ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:20988  CAPLUS
DOCUMENT NUMBER:          140:73576
TITLE:                    Oncolytic viruses as phenotyping agents for neoplasms
                          and use for tumor diagnosis and therapy
INVENTOR(S):              Thompson, Bradley G.; Coffey, Matthew C.
PATENT ASSIGNEE(S):       Oncolytics Biotech, Inc., Can.
SOURCE:                   PCT Int. Appl., 31 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2004003562      A2   20040108       WO 2003-CA951    20030625
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
```

```
=> cyclosporin
L38       38832 CYCLOSPORIN

=> L1 and L38
L39         282 L1 AND L38

=> L38 and L2
L40           3 L38 AND L2

=> D L40 IBIB ABS 1-3
```

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004029112 A1 20040212 US 2003-602024 20030624
PRIORITY APPLN. INFO.: US 2002-392031P P 20020628
US 2003-443188P P 20030129

AB The present invention provides a method of diagnosing neoplasms having a particular phenotype by using oncolytic viruses that selectively replicate in neoplasms having the particular phenotype. For example, **reovirus** does not replicate in normal cells. However, **reovirus** selectively replicate in cells with an activated ras pathway, which leads to death of these cells. Therefore, a cell which becomes neoplastic due to, at least in part, elevated ras pathway activities can be diagnosed by its susceptibility to **reovirus** replication. This invention can further be applied, using other oncolytic viruses, to the diagnosis and/or treatment of other tumors, such as **interferon**-sensitive tumors, p53-deficient tumors and Rb-deficient tumors. Kits useful in the diagnosis or treatment disclosed herein are also provided.

L12 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:657956 CAPLUS
DOCUMENT NUMBER: 137:179862
TITLE: Sensitization of chemotherapeutic agent resistant neoplastic cells with **reovirus**
INVENTOR(S): Coffey, Matthew C.; Thompson, Bradley G.
PATENT ASSIGNEE(S): Oncolytics Biotech Inc., Can.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066040	A2	20020829	WO 2002-CA201	20020219
WO 2002066040	C1	20030320		
WO 2002066040	A3	20030530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002168344	A1	20021114	US 2002-76074	20020215
EP 1361884	A2	20031119	EP 2002-701122	20020219

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2001-270363P P 20010220
WO 2002-CA201 W 20020219

AB The present invention relates to a method of increasing the sensitivity of neoplastic cells to chemotherapeutic agents by using **reovirus**, a method of treating proliferative disorders with **reovirus** and chemotherapeutic agents, and a method for preventing a neoplasm from developing drug resistance to chemotherapeutic agents.

L12 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:241289 CAPLUS
DOCUMENT NUMBER: 136:257234
TITLE: Purging of cells using viruses

INVENTOR(S): Atkins, Harold L.; Bell, John C.; Heilman, Conrad J.; Lichty, Brian D.; Lorence, Robert M.; Roberts, Michael S.; Stojdl, David F.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037543	A1	20020328	US 2001-888626	20010626
WO 2002000233	A2	20020103	WO 2001-US41121	20010626
WO 2002000233	A3	20020822		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1297121	A2	20030402	EP 2001-957529	20010626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501200	T2	20040115	JP 2002-505015	20010626

PRIORITY APPLN. INFO.: US 2000-214014P P 20000626
WO 2001-US41121 W 20010626

AB The subject invention relates to viruses that are able to purge (reduce or eliminate) undesirable cells in a mixt. of cells. Undesirable cells can include neoplastic cells, cells mediating graft-vs. host diseases, and autoimmune cells. The subject invention also relates to the purging of undesirable cells from bone marrow or peripheral blood cell harvests in the treatment of mammals including **cancer** patients, transplant recipients, and patients with autoimmune disease. Vesicular stomatitis virus (VSV) Indiana serotype showed selective destruction of leukemic cells in a mixed population of normal marrow contg. leukemic OCI/AML3 cells.

L12 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:507867 CAPLUS
DOCUMENT NUMBER: 135:91527
TITLE: Tissue-specific DNA delivery via M cell-directed vaccines, and enhanced in vivo mucosal IgA and T cell responses resulting therefrom
INVENTOR(S): Pascual, David W.
PATENT ASSIGNEE(S): Research and Development Institute, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049867	A1	20010712	WO 2001-US426	20010108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,				

TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1257654 A1 20021120 EP 2001-901811 20010108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

US 2004033486 A1 20040219 US 2002-169492 20021021

PRIORITY APPLN. INFO.: US 2000-174786P P 20000106
WO 2001-US426 W 20010108

AB This invention provides a vaccine that can direct gene transfer to follicle assocd. epithelium or M cells to induce mucosal immunity using M cell ligands for receptor-mediated endocytosis. In particular, the invention is directed to polybasic amino acid-conjugated M cell ligand-DNA complex vaccine compns. that are internalized by receptor-dependent endocytosis, thereby rendering transfection to be minimally toxic. By chem. coupling M cell ligands (preferably **reovirus** protein .alpha.1 or an adhesin of Salmonella or polio virus) to a polymeric chain of basic amino acids (preferably polylysine), and to DNA can be delivered to appropriate tissue types to obtain enhanced in vivo mucosal IgA antibody and T cell responses against an encoded antigen. To demonstrate the efficacy of the vaccine design, inventors have used reporter genes for .beta.-galactosidase and luciferase, as well as vaccine antigens derived from human immunodeficiency virus (HIV) and Brucella, to demonstrate differences in mucosal IgA antibody responses between animals vaccinated with DNA only and those vaccinated with the conjugated DNA complexes of the invention. The DNA vaccines of the invention induce improved mucosal IgA antibody responses and promote sustained CTL responses. Further, methods are described for immunizing animal and human subjects against bacterial, viral, parasitic, fungal infectious agents or **cancer**, and methods for assaying mucosal immunity using this vaccine.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:70348 BIOSIS
DOCUMENT NUMBER: PREV200300070348
TITLE: RNA viruses as virotherapy agents.
AUTHOR(S): Russell, Stephen J. [Reprint Author]
CORPORATE SOURCE: Molecular Medicine Program, Mayo Clinic, 200 First Street, SW, Rochester, MN, 55905, USA
sjr@mayo.edu
SOURCE: Cancer Gene Therapy, (December 2002) Vol. 9, No. 12, pp. 961-966. print.
ISSN: 0929-1903 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB RNA viruses are rapidly emerging as extraordinarily promising agents for oncolytic virotherapy. Integral to the lifecycles of all RNA viruses is the formation of double-stranded RNA, which activates a spectrum of cellular defense mechanisms including the activation of PKR and the release of **interferon**. Tumors are frequently defective in their PKR signaling and **interferon** response pathways, and therefore provide a relatively permissive substrate for the propagation of RNA viruses. For most of the oncolytic RNA viruses currently under study, tumor specificity is either a natural characteristic of the virus, or a serendipitous consequence of adapting the virus to propagate in human tumor cell lines. Further refinement and optimization of these oncolytic agents can be achieved through virus engineering. This article provides a summary of the current status of oncolytic virotherapy efforts for seven different RNA viruses, namely, mumps, Newcastle disease virus, measles

L12 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:197821 BIOSIS
DOCUMENT NUMBER: PREV199598212121
TITLE: Replacement of **reovirus** type 3 by recombinant **interferon**-alpha in an effective murine EL-4 tumor immunotherapy.
AUTHOR(S): Steele, T.; Hauser, C.
CORPORATE SOURCE: Mercer Univ. Sch. Med., Macon, GA 31207, USA
SOURCE: FASEB Journal, (1995) Vol. 9, No. 4, pp. A1044.
Meeting Info.: Experimental Biology 95, Part II. Atlanta, Georgia, USA. April 9-13, 1995.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1995
Last Updated on STN: 5 May 1995

L12 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:70348 BIOSIS
DOCUMENT NUMBER: PREV200300070348
TITLE: RNA viruses as virotherapy agents.
AUTHOR(S): Russell, Stephen J. [Reprint Author]
CORPORATE SOURCE: Molecular Medicine Program, Mayo Clinic, 200 First Street, SW, Rochester, MN, 55905, USA
sjr@mayo.edu
SOURCE: Cancer Gene Therapy, (December 2002) Vol. 9, No. 12, pp. 961-966. print.
ISSN: 0929-1903 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2003
Last Updated on STN: 29 Jan 2003

AB RNA viruses are rapidly emerging as extraordinarily promising agents for oncolytic virotherapy. Integral to the lifecycles of all RNA viruses is the formation of double-stranded RNA, which activates a spectrum of cellular defense mechanisms including the activation of PKR and the release of **interferon**. Tumors are frequently defective in their PKR signaling and **interferon** response pathways, and therefore provide a relatively permissive substrate for the propagation of RNA viruses. For most of the oncolytic RNA viruses currently under study, tumor specificity is either a natural characteristic of the virus, or a serendipitous consequence of adapting the virus to propagate in human tumor cell lines. Further refinement and optimization of these oncolytic agents can be achieved through virus engineering. This article provides a summary of the current status of oncolytic virotherapy efforts for seven different RNA viruses, namely, mumps, Newcastle disease virus, measles virus, vesicular stomatitis virus, influenza, **reovirus**, and poliovirus.

L12 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:507867 CAPLUS
DOCUMENT NUMBER: 135:91527
TITLE: Tissue-specific DNA delivery via M cell-directed vaccines, and enhanced in vivo mucosal IgA and T cell responses resulting therefrom
INVENTOR(S): Pascual, David W.
PATENT ASSIGNEE(S): Research and Development Institute, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049867	A1	20010712	WO 2001-US426	20010108
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1257654	A1	20021120	EP 2001-901811	20010108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004033486	A1	20040219	US 2002-169492	20021021

PRIORITY APPLN. INFO.: US 2000-174786P P 20000106
WO 2001-US426 W 20010108

AB This invention provides a vaccine that can direct gene transfer to follicle associated epithelium or M cells to induce mucosal immunity using M cell ligands for receptor-mediated endocytosis. In particular, the invention is directed to polybasic amino acid-conjugated M cell ligand-DNA complex vaccine compns. that are internalized by receptor-dependent endocytosis, thereby rendering transfection to be minimally toxic. By chemical coupling M cell ligands (preferably **reovirus** protein α1 or an adhesin of Salmonella or polio virus) to a polymeric chain of basic amino acids (preferably polylysine), and to DNA can be delivered to appropriate tissue types to obtain enhanced in vivo mucosal IgA antibody and T cell responses against an encoded antigen. To demonstrate the efficacy of the vaccine design, inventors have used reporter genes for β-galactosidase and luciferase, as well as vaccine antigens derived from human immunodeficiency virus (HIV) and Brucella, to demonstrate differences in mucosal IgA antibody responses between animals vaccinated with DNA only and those vaccinated with the conjugated DNA complexes of the invention. The DNA vaccines of the invention induce improved mucosal IgA antibody responses and promote sustained CTL responses. Further, methods are described for immunizing animal and human subjects against bacterial, viral, parasitic, fungal infectious agents or **cancer**, and methods for assaying mucosal immunity using this vaccine.

```
=> reovirus
L4         5716 REOVIRUS

=> chemothrapy
L5           20 CHEMOTHRAPY

=> cisplatin
L6        71217 CISPLATIN

=> L4 and L6
L7            2 L4 AND L6

=> interferon
L8       253270 INTERFERON

=> L8 and L4
L9          473 L8 AND L4

=> oncolysis
L10         445 ONCOLYSIS

=> L9 and L10
L11           0 L9 AND L10

=> cancer and L9
L12           7 CANCER AND L9

=> D L12 IBIB AB 1-7
```

virus, vesicular stomatitis virus, influenza, **reovirus**, and poliovirus.

L12 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:197821 BIOSIS
DOCUMENT NUMBER: PREV199598212121
TITLE: Replacement of **reovirus** type 3 by recombinant **interferon**-alpha in an effective murine EL-4 tumor immunotherapy.
AUTHOR(S): Steele, T.; Hauser, C.
CORPORATE SOURCE: Mercer Univ. Sch. Med., Macon, GA 31207, USA
SOURCE: FASEB Journal, (1995) Vol. 9, No. 4, pp. A1044.
Meeting Info.: Experimental Biology 95, Part II. Atlanta, Georgia, USA. April 9-13, 1995.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1995
Last Updated on STN: 5 May 1995

L12 ANSWER 7 OF 7 CANCERLIT on STN
ACCESSION NUMBER: 77807433 CANCERLIT
DOCUMENT NUMBER: 77807433
TITLE: ANTIVIRAL ACTIVITIES OF 4'-(9-ACRIDINYLAMINO)-METHANESULFON-M- ANISIDE (SN11841).
AUTHOR: Byrd D M
CORPORATE SOURCE: Dept. Pharmacology, Univ. Oklahoma, Coll. Medicine, Oklahoma City, OK 73190.
SOURCE: Ann N Y Acad Sci, (1977) 284 463-471.
ISSN: 0077-8923.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Hierarchical Classification of Proteins
ENTRY MONTH: 197709
ENTRY DATE: Entered STN: 19941107
Last Updated on STN: 19941107

AB Anti-**cancer** and antiviral effects of 4'-(9-acridinylamino) -methanesulfon -M- anisidide (SN11841) were studied. An approx LD50 of 25 mg/kg was determined for BALB/c mice given a single ip dose. Rauscher leukemia virus (RLV)-induced splenomegaly in BALB/c mice was inhibited by SN11841 doses (13. to 5.0 mg/kg, ip) given 1 day post-RLV inoculation. There were significant life span increases in mice given 6.3 mg/kg; however, there were no long-term survivors. Viremia, as determined by the relative ability of spleen homogenates to induce splenomegaly, was inhibited to a greater extent than splenomegaly in mice treated with 12.5 mg/kg SN11841. SN11841 did not inhibit XC plaque formation induced by Rauscher, Moloney or 334c leukemia viruses. SN11841 variably inhibited the replication of vaccinia virus in HeLa cell cultures over a 10-fold concentration range but was found inactive against herpes simplex (type 1), vesicular stomatitis, encephalomyocarditis or **reoviruses**. Pretreatment of cells with SN11841 did not inhibit vaccinia reproduction, and pretreatment of L929 cells with SN11841 did not induce murine **interferon**. Incubation of virus particles with SN11841 inhibited RLV virion-associated RNA-dependent DNA polymerase at <= 500 ug/ml but did not affect the ability of the virus to induce splenomegaly or mortality. (21 Refs)

=> oncolysis
L13 445 ONCOLYSIS

=> reovirus
L14 5716 REOVIRUS

=> L13 and l14
L15 32 L13 AND L14

=> D L15 IBIB ABS 1-32

L15 ANSWER 1 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:513612 CAPLUS
DOCUMENT NUMBER: 139:362492
TITLE: **Reovirus oncolysis** as a novel purging strategy for autologous stem cell transplantation
AUTHOR(S): Thirukkumaran, Chandini M.; Luider, Joanne M.; Stewart, Douglas A.; Cheng, Tina; Lupichuk, Sasha M.; Nodwell, Michael J.; Russell, James A.; Auer, Iwona A.; Morris, Donald G.
CORPORATE SOURCE: Calgary Laboratory Services, Calgary, AB, Can.
SOURCE: Blood (2003), 102(1), 377-387
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hematol. stem cell rescue after high-dose cytotoxic therapy is extensively used for the treatment of many hematopoietic and solid cancers. Gene marking studies suggest that occult tumor cells within the autograft may contribute to clin. relapse. To date purging of autografts contaminated with cancer cells was unsuccessful. The selective oncolytic property of **reovirus** against myriad malignant histologies in in vitro, in vivo, and ex vivo systems was previously demonstrated. In the present study the authors have shown that **reovirus** can successfully purge cancer cells within autografts. Human monocytic and myeloma cell lines as well as enriched ex vivo lymphoma, myeloma, and Waldenstroem macroglobulinemia patient tumor specimens were used in an exptl. purging model. Viability of the cell lines or purified ex vivo tumor cells of diffuse large B-cell lymphoma, chronic lymphocytic leukemia, Waldenstroem macroglobulinemia, and small lymphocytic lymphoma was significantly reduced after **reovirus** treatment. Further, [35S]-methionine labeling and sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) of cellular proteins demonstrated **reovirus** protein synthesis and disruption of host cell protein synthesis as early as 24 h. , Admixts. of apheresis product with the above-mentioned tumor cells and cell lines treated with **reovirus** showed complete purging of disease. In contrast, **reovirus** purging of enriched ex vivo multiple myeloma, Burkitt lymphoma, and follicular lymphoma was incomplete. The oncolytic action of **reovirus** did not affect CD34+ stem cells or their long-term colony-forming assays even after granulocyte colony-stimulating factor (G-CSF) stimulation. The authors' results indicate the ex vivo use of an unattenuated oncolytic virus as an attractive purging strategy for autologous stem cell transplantations.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:463181 CAPLUS
DOCUMENT NUMBER: 139:358182
TITLE: **Reovirus** Prolongs Survival and Reduces the Frequency of Spinal and Leptomeningeal Metastases from Medulloblastoma
AUTHOR(S): Yang, Wen Qing; Senger, Donna; Muzik, Huong; Shi, Zhong Qiao; Johnson, Denise; Brasher, Penny M. A.; Rewcastle, N. Barry; Hamilton, Mark; Rutka, Jim; Wolff, Johannes; Wetmore, Cynthia; Curran, Tom; Lee, Patrick W. K.; Forsyth, Peter A.
CORPORATE SOURCE: Departments of Oncology and Clinical Neurosciences, University of Calgary and Tom Baker Cancer Centre, Calgary, AB, T2N 4N2, Can.

SOURCE: Cancer Research (2003), 63(12), 3162-3172
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Medulloblastoma (MB), the most common pediatric brain tumor, is a highly malignant disease with a 5-yr survival rate of only 60%. Tumor cells invade surrounding tissue and disseminate through cerebral spinal fluid, making treatment difficult. Human **reovirus** type 3 exploits an activated Ras pathway in tumor cells to support productive infection as an oncolytic virus. Here, we examd. the ability of human **reovirus** to kill MB cells lines and surgical specimens in vitro and inhibit tumor growth/metastases in vivo. Most human MB cell lines tested (five of seven = 71.4%), two MB cell lines derived from spontaneously arising tumors in Patched-1+/- mice (two of two = 100%) and three MB primary cultures derived from surgical specimens, were susceptible to **reovirus** infection. **Reovirus** was internalized and transcribed in both susceptible and resistant cell lines. However, viral protein synthesis was restricted to cell lines with higher levels of activated Ras, suggesting that Ras plays a crit. role in **reovirus oncolysis** in MB. Using an in vivo Daoy orthotopic animal model, we found that a single i.t. injection of **reovirus** dramatically prolonged survival compared with controls (160 vs. 70 days, resp.; P = 0.0003). Repeating this expt. with GFP-labeled Daoy cells and multiple i.t. administrations of **reovirus**, we again found prolonged survival and a dramatic redn. in spinal and leptomeningeal metastases (66.7% in control injections vs. 0.0% in the live virus group). These data suggest that this oncolytic virus may be a potentially effective novel therapy against human MB. Its ability to reduce metastases to the spinal cord could allow a redn. in the dose/field of total neuraxis cerebral-spinal radiotherapy currently used to treat/prevent cerebral spinal fluid dissemination.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:330657 CAPLUS
TITLE: Selective **reovirus** killing of bladder cancer in a co-culture spheroid model
AUTHOR(S): Kilani, Ruhangiz T.; Tamimi, Yahya; Hanel, Erich G.; Wong, Kevin K.; Karmali, Shahzeer; Lee, Patrick W. K.; Moore, Ronald B.
CORPORATE SOURCE: Cross Cancer Institute, Department of Surgery, Divisions of Experimental Surgery and Oncology, University of Alberta and Department of Oncology, Edmonton, AB, T6G 1Z2, Can.
SOURCE: Virus Research (2003), 93(1), 1-12
CODEN: VIREDF; ISSN: 0168-1702
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Up to 50% of the transitional cell carcinomas (TCC) express an activated EGF pathway involving MAP/MEK and RAF kinase thus providing a novel means to selectively eliminate transformed cells expressing such proteins. This EGF pathway expression phenotype was also confirmed in our MGH-U3 and room temp.-112 human TCC cell lines, which makes them a suitable model target for the **reovirus oncolysis**. We report here on an in vitro assay of co-culture spheroids using either human or rat TCC cells with their corresponding fibroblasts to examine the potential of viral selective lysis for TCC. **Reovirus**, a respiratory enteric orphan virus, which mammals are exposed to early in life, was used in this study. Selective killing of transformed vs. normal cells was assayed by time-lapse photog., vital dye staining, immunohistochem., and MTT assay. In this in vitro bladder cancer model, **reovirus** selectively destroyed the transformed cells by lysis or induction of apoptosis. Based

on these findings we have initiated an in vivo pre-clin. study on intravesical administration of **reovirus** in an animal model to further explore the effect of **reovirus**-mediated **oncolysis** of TCC.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:218807 CAPLUS
DOCUMENT NUMBER: 138:219917
TITLE: Intraperitoneal oncolytic and tumor vaccination therapy with replication-competent recombinant virus: The herpes paradigm
AUTHOR(S): Coukos, George; Courreges, Maria Cecilia; Benencia, Fabian
CORPORATE SOURCE: Center for Research on Reproduction and Women's Health, Department of Obstetrics and Gynecology, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Current Gene Therapy (2003), 3(2), 113-125
CODEN: CGTUAH; ISSN: 1566-5232
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The biol. therapy of tumors using live viruses was first proposed a century ago but was abandoned due to potential virulence of wild-type strains. Thanks to advances in recombinant technol., replication-restricted strains have been genetically engineered, which replicate selectively within tumor cells. Examples include replication-competent mutants of herpes simplex virus (HSV), adenovirus, vesicular stomatitis virus, **reovirus** and measles virus. Replication-restricted oncolytic viruses are able to propagate selectively within solid tumor nodules exerting direct antitumor activity by killing infected tumor cells at the completion of a replicative cycle. In the process, they generate an intratumoral inflammatory response, which under the appropriate circumstances, may trigger the activation of an adaptive antitumor immune response, a process that has been named in situ tumor vaccination. Recombinant HSV may offer distinct advantages in oncolytic therapy of epithelial tumors. HSV is highly infectious to tumors of epithelial origin, resulting in high efficacy, there is considerable redundancy in HSV receptors, which makes the loss of HSV receptors by tumors due to mutations less likely and potent anti-herpetic drugs are com. available, which may be used clin. to control undesired side effects. Herewith the authors describe the use of oncolytic viral therapy against i.p. malignancies with special emphasis on oncolytic herpes simplex virus. The authors review the preclin. evidence on the efficacy and safety of i.p. applications of HSV and discuss the rationale for its use for oncolytic therapy and in situ tumor vaccination of i.p. tumors.
REFERENCE COUNT: 149 THERE ARE 149 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:932642 CAPLUS
DOCUMENT NUMBER: 138:378737
TITLE: **Reovirus** therapy of lymphoid malignancies
AUTHOR(S): Alain, Tommy; Hirasawa, Kensuke; Pon, Kelly J.; Nishikawa, Sandra G.; Urbanski, Stefan J.; Auer, Yvonna; Luider, Joanne; Martin, Anita; Johnston, Randal N.; Janowska-Wieczorek, Anna; Lee, Patrick W. K.; Kossakowska, Anna E.
CORPORATE SOURCE: Calgary Laboratory Services, AB, Can.
SOURCE: Blood (2002), 100(12), 4146-4153
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Reoviruses** infect cells that manifest an activated Ras-signaling pathway, and have been shown to effectively destroy many different types of neoplastic cells, including those derived from brain, breast, colon, ovaries, and prostate. In this study, we investigated the **reovirus** as a potential therapeutic agent against lymphoid malignancies. A total of 9 lymphoid cell lines and 27 primary human lymphoid malignancies, as well as normal lymphocytes and hematopoietic stem/progenitor cells, were tested for susceptibility to **reovirus** infection. For in vitro studies, the cells were challenged with **reovirus** (serotype 3 Dearing), and viral infection was assessed by cytopathic effects, viability, viral protein synthesis, and progeny virus prodn. We present evidence of efficient **reovirus** infection and cell lysis in the diffuse large B-cell lymphoma cell lines and Burkitt lymphoma cell lines Raji and CA46 but not Daudi, Ramos, or ST486. Moreover, when Raji and Daudi cell lines were grown s.c. in severe combined immunodeficient/nonobese diabetic (SCID/NOD) mice and subsequently injected with **reovirus** intratumorally or i.v., significant regression was obsd. in the Raji-induced, but not the Daudi-induced, tumors, which is consistent with the in vitro results. Susceptibility to **reovirus** infection was also detected in 21 of the 27 primary lymphoid neoplasias tested but not in the normal lymphocytes or hematopoietic stem/progenitor cells. Our results suggest that **reovirus** may be an effective agent against several types of human lymphoid malignancies.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:559472 CAPLUS
DOCUMENT NUMBER: 138:130366
TITLE: Viral **oncolysis**
AUTHOR(S): Mullen, John T.; Tanabe, Kenneth K.
CORPORATE SOURCE: Division of Surgical Oncology, Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114-2696, USA
SOURCE: Oncologist (2002), 7(2), 106-119
CODEN: OCOLF6; ISSN: 1083-7159
PUBLISHER: AlphaMed Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The concept of using replicating viruses as anticancer agents is not a new one, but the ability to genetically modify these viruses into increasingly potent and tumor-specific vectors is a recent phenomenon. As more is learned about the functions of viral gene products in controlling the mammalian cell cycle and in disabling cellular defense mechanisms, specific viral functions can be augmented or eliminated to enhance antineoplastic efficacy. In this article, general mechanisms by which oncolytic viruses achieve their antitumor efficacy and specificity are reviewed. The paradoxical roles of the immune response are addressed with respect to oncolytic viral therapy, as it, on one hand, impedes the spread of viral infection, and on the other, augments tumor cell destruction through the recruitment of T cells vaccinated against tumor antigens. The most commonly used oncolytic viruses are each reviewed in turn, including adenoviruses, herpes simplex viruses, vaccinia viruses, **reoviruses**, and Newcastle disease viruses. Special attention is focused on the unique biol. of each of these viruses as well as the status of several of these mutants in clin. trials.
REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:420834 CAPLUS
DOCUMENT NUMBER: 137:332821

TITLE: **Reovirus oncolysis** of human breast cancer
AUTHOR(S): Norman, Kara L.; Coffey, Matthew C.; Hirasawa, Kensuke; Demetrick, Douglas J.; Nishikawa, Sandra G.; DiFrancesco, Lisa M.; Strong, James E.; Lee, Patrick W. K.
CORPORATE SOURCE: Cancer Biology Research Group, Faculty of Medicine, Department of Microbiology and Infectious Diseases, University of Calgary, Calgary, AB, T2N 4N1, Can.
SOURCE: Human Gene Therapy (2002), 13(5), 641-652
CODEN: HGTHE3; ISSN: 1043-0342
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have previously shown that human **reovirus** replication is restricted to cells with an activated Ras pathway, and that **reovirus** could be used as an effective oncolytic agent against human glioblastoma xenografts. This study examines in more detail the feasibility of **reovirus** as a therapeutic for breast cancer, a subset of cancer in which direct activating mutations in the ras proto-oncogene are rare, and yet where unregulated stimulation of Ras signaling pathways is important in the pathogenesis of the disease. The authors demonstrate herein the efficient lysis of breast tumor-derived cell lines by the virus, whereas normal breast cells resist infection in vitro. In vivo studies of **reovirus** breast cancer therapy reveal that viral administration could cause tumor regression in an MDA-MB-435S mammary fat pad model in severe combined immunodeficient mice. **Reovirus** could also effect regression of tumors remote from the injection site in an MDA-MB-468 bilateral tumor model, raising the possibility of systemic therapy of breast cancer by the oncolytic agent. Finally, the ability of **reovirus** to act against primary breast tumor samples not propagated as cell lines was evaluated; the authors found that **reovirus** could indeed replicate in ex vivo surgical specimens. Overall, **reovirus** shows promise as a potential breast cancer therapeutic.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:509668 CAPLUS
DOCUMENT NUMBER: 136:241196
TITLE: **Reovirus** as an oncolytic agent against experimental human malignant gliomas
AUTHOR(S): Wilcox, M. Elizabeth; Yang, WenQing; Senger, Donna; Rewcastle, N. Barry; Morris, Donald G.; Brasher, Penny M. A.; Shi, Z. Qiao; Johnston, Randal N.; Nishikawa, Sandi; Lee, P. W. K.; Forsyth, Peter A.
CORPORATE SOURCE: Departments of Oncology and Clinical Neurosciences, University of Calgary, AB, Can.
SOURCE: Journal of the National Cancer Institute (2001), 93(12), 903-912
CODEN: JNCIEQ; ISSN: 0027-8874
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Reovirus** is a naturally occurring oncolytic virus that usurps activated Ras-signaling pathways of tumor cells for its replication. Ras pathways are activated in most malignant gliomas via upstream signaling by receptor tyrosine kinases. The purpose of this study was to det. the effectiveness of **reovirus** as an exptl. treatment for malignant gliomas. We investigated whether **reovirus** would infect and lyse human glioma cell lines in vitro. We also tested the effect of injecting live **reovirus** in vivo on human gliomas grown s.c. or orthotopically (i.e., intracerebrally) in mice. Finally, **reovirus** was tested ex vivo against low-passage cell lines derived from human

glioma specimens. All P values were two-sided. **Reovirus** killed 20 (83%) of 24 established malignant glioma cell lines tested. It caused a dramatic and often complete tumor regression in vivo in two s.c. (P =.0002 for both U251N and U87) and in two intracerebral (P =.0004 for U251N and P =.0009 for U87) human malignant glioma mouse models. As expected, serious toxic effects were found in these severely immunocompromised hosts. In a less immunocompromised mouse model, a single intratumoral inoculation of live **reovirus** led to a dramatic prolongation of survival (compared with control mice treated with dead virus; log-rank test, P<.0001 for both U251N and U87 cell lines). The animals treated with live virus also appeared to be healthier and gained body wt. (P =.0001). We then tested the ability of **reovirus** to infect and kill primary cultures of brain tumors removed from patients and found that it killed nine (100%) of nine glioma specimens but none of the cultured meningiomas. **Reovirus** has potent activity against human malignant gliomas in vitro, in vivo, and ex vivo. **Oncolysis** with **reovirus** may be a potentially useful treatment for a broad range of human cancers.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:752081 CAPLUS
DOCUMENT NUMBER: 133:313603
TITLE: **Reovirus** for the treatment of cellular proliferative disorders
INVENTOR(S): Lee, Patrick W. K.; Strong, James; Coffey, Matthew C.
PATENT ASSIGNEE(S): Oncolytics Biotech Inc., Can.
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 911,383.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6136307	A	20001024	US 1999-256824	19990224
EP 1213023	A1	20020612	EP 2001-130285	19980812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PT 1003534	T	20020830	PT 1998-940002	19980812
ES 2157870	T3	20021016	ES 1998-940002	19980812
CA 2360833	AA	20000831	CA 2000-2360833	20000218
WO 2000050051	A2	20000831	WO 2000-CA178	20000218
WO 2000050051	A3	20001228		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1156813	A2	20011128	EP 2000-906094	20000218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002537344	T2	20021105	JP 2000-600662	20000218
US 6344195	B1	20020205	US 2000-569865	20000512
US 6455038	B1	20020924	US 2000-594343	20000615
US 6565831	B1	20030520	US 2000-636597	20000810
US 2002187125	A1	20021212	US 2001-989101	20011121
US 2003003080	A1	20030102	US 2002-218452	20020815
US 2003215443	A1	20031120	US 2003-401032	20030328

PRIORITY APPLN. INFO.: US 1997-911383 A2 19970813
EP 1998-940002 A3 19980812
US 1999-256824 A 19990224
WO 2000-CA178 W 20000218
US 2000-569865 A1 20000512
US 2000-594343 A1 20000615
US 2000-636597 A1 20000810

AB Methods for treating proliferative disorders, by administering **reovirus** to a Ras-mediated proliferative disorder, are disclosed. The **reovirus** is administered so that it ultimately directly contacts ras-mediated proliferating cells. Proliferative disorders include but are not limited to neoplasms. Human **reovirus**, non-human mammalian **reovirus**, and/or avian **reovirus** can be used. If the **reovirus** is human **reovirus**, serotype 1 (e.g., strain Lang), serotype 2 (e.g., strain Jones), serotype 3 (e.g., strain Dearing or strain Abney), as well as other serotypes or strains of **reovirus** can be used. Combinations of more than one type and/or strain of **reovirus** can be used, as can **reovirus** from different species of animal. Either solid neoplasms or hematopoietic neoplasms can be treated.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 32 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:454661 CAPLUS
DOCUMENT NUMBER: 129:160072
TITLE: The molecular basis of viral **oncolysis**: usurpation of the Ras signaling pathway by **reovirus**
AUTHOR(S): Strong, James E.; Coffey, Matthew C.; Tang, Damu; Sabinin, Pauline; Lee, Patrick W. K.
CORPORATE SOURCE: Department of Microbiology and Infectious Diseases, University of Calgary Health Sciences Centre, Calgary, AB, T2N 4N1, Can.
SOURCE: EMBO Journal (1998), 17(12), 3351-3362
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB NIH-3T3 cells, which are resistant to **reovirus** infection, became susceptible when transformed with activated Sos or Ras. Restriction of **reovirus** proliferation in untransformed NIH-3T3 cells was not at the level of viral gene transcription, but rather at the level of viral protein synthesis. An anal. of cell lysates revealed that a 65 kDa protein was phosphorylated in untransformed NIH-3T3 cells, but only after infection with **reovirus**. This protein was not phosphorylated in infected or uninfected transformed cells. The 65 kDa protein was detd. to be the double-stranded RNA-activated protein kinase (PKR), whose phosphorylation leads to translation inhibition. Inhibition of PKR phosphorylation by 2-aminopurine, or deletion of the Pkr gene, led to drastic enhancement of **reovirus** protein synthesis in untransformed cells. The emerging picture is one in which early viral transcripts trigger PKR phosphorylation in untransformed cells, which in turn leads to inhibition of translation of viral genes; this phosphorylation event is blocked by an element(s) in the Ras pathway in the transformed cells, allowing viral protein synthesis to ensue. The usurpation of the Ras signaling pathway therefore constitutes the basis of **reovirus oncolysis**.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:476408 BIOSIS
DOCUMENT NUMBER: PREV200300476408
TITLE: Increased expression of c-Myc sensitizes cells to

reovirus-induced **oncolysis**.
AUTHOR(S): Egan, Cay [Reprint Author]; Kim, Manbok; Nishikawa, Sandi; Helbing, Caren; Ricci, Stacey; El-Deiry, Wafik; Forsyth, Peter; Kossakowska, Anna; Lee, Patrick; Johnston, Randal
CORPORATE SOURCE: University of Calgary, Calgary, AB, Canada
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 1101. print.
Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003

L15 ANSWER 12 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:475208 BIOSIS
DOCUMENT NUMBER: PREV200300475208
TITLE: Mechanisms of resistance to reoviral **oncolysis**.
AUTHOR(S): Kim, Manbok [Reprint Author]; Egan, Cay [Reprint Author]; Lee, Patrick W. K. [Reprint Author]; Forsyth, Peter A. J. [Reprint Author]; Johnston, Randal N. [Reprint Author]
CORPORATE SOURCE: Cancer Biology Research Group, University of Calgary, Calgary, AB, Canada
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (July 2003) Vol. 44, pp. 328. print.
Meeting Info.: 94th Annual Meeting of the American Association for Cancer Research. Washington, DC, USA. July 11-14, 2003.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Oct 2003
Last Updated on STN: 15 Oct 2003

L15 ANSWER 13 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:367925 BIOSIS
DOCUMENT NUMBER: PREV200300367925
TITLE: Flowcytometric Analysis of Reo-Virus Induced **Oncolysis** in AML Cell-Lines.
AUTHOR(S): Fibich, Christian [Reprint Author]; Norman, Kara; Alain, Thomas; Lee, Patrick W. K.; Brown, Christopher
CORPORATE SOURCE: Dept. of Medicine, Tom-Baker-Cancer-Centre, Calgary, AB, Canada
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 4441. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003
AB Introduction: Reo-virus type 3, Dearing (RV) is a double-stranded RNA-virus that is capable of selectively inducing apoptosis in tumor-cells depending on activated intracellular signaling-mechanism downstream of RAS1. The intention of this study was to investigate the sensitivity of a fluorescin-conjugated rabbit-AS in detecting infection and replication in sensitive and resistant cell-lines and the capability of RV to induce

apoptosis in AML cell-lines. Methods and cell-lines: U 937 (ATCC 1593.2) is a human monoblastoid-cell-line, K562 (ATCC CCL-243) is an undifferentiated myloid leukemia with erythroblastoid features. Daudi is a lymphoblastoid CD 20+ cell-line that has previously shown to be RV-resistant. All cell-lines were maintained in RPMI-1640/10% FCS without phenol-red. Prior to infection, cells were washed in cold medium and kept on ice to synchronize infection. RV was then added at 40 pfu/cell. Cells were cultured at 0.5x106cell/ml and harvested at the given time-points. Polyclonal antiserum (AS) against RV from rabbit was protein-G purified and conjugated to Carboxyfluorescein succinimidyl ester (CSFE, Molecular Probes). For RV-staining cells were fixed in 5% formaldehyde and permeabilised with 0.5% saponin/1% BSA. Stained cells were analysed on a Becton-Dickinson FACSCAN. To test the sensitivity of the assay, RV was titrated onto ice-cold K562-cells in concentrations from 1-2000 pfu/cell. Cells were incubated for 10' and then fixed, stained and analysed as above. Apoptosis was measured by PE-conjugated Annexin V-binding (Becton-Dickinson, San Jose, Ca.) and Caspase-8 activation (FAM-LETD-FMK, Intergen, Norcross, GA). Coculture was performed with Daudi and K562 at ratios of 1:1 and 95:5, cells were analysed 24h post infection. Specificity was analysed through backgating on Daudi by CD20. Results: Sensitivity of the assay: A significant shift in fluorescence above control was seen starting at 10 pfu of RV, a linear increase in fluorescence was seen up to 2000 pfu of RV. Fluorescence for RV was detectable above background of cells infected with UV-inactivated RV in both cell-lines starting at 4h post infection and increased 67-fold in U937 and 48-fold in K562 by 24h post-infection. In co-culture of resistant and sensitive cells sensitive cells were clearly detectable by RV-stain alone. Both K 562 and U937 cell were sensitive to RV-induced apoptosis. In U 937 at 24h 62+-9% and at 48 99.2% of cells were apoptotic. In K562 at 24h 18.7+-5.7, at 48h 56.2+- and at 72h 98.88% of cells were apoptotic. Apoptosis in was accompagnied by Caspase-8 expression. RV significantly inhibited proliferation of both cell lines compared to mock-infected controls or resistant cell-line controls (Daudi). A decrease in proliferation was detectable after 12h in U 937 (122% vs 135% in ctl.) and at 24h in K 562. At the final timepoints with no viable cells left in the infected cell-population, total proliferation was decreased by 65% in U 937 and 79.4% in K562 as compared to mock-infected or UV-inactivated virus infected controls. Discussion: The AML cell-lines tested are highly susceptible to RV induced apoptosis in vitro. This flow-cytometric assay provides a rapid and sensitive method to detect RV in susceptible cells and distinguish sensitive from resistant cells. Further experiments in primary AML and animal models are pending.

L15 ANSWER 14 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:334533 BIOSIS
DOCUMENT NUMBER: PREV200300334533
TITLE: **Reovirus oncolysis** as a novel purging strategy for autologous stem cell transplantation.
AUTHOR(S): Thirukkumaran, Chandini M.; Luider, Joanne M.; Stewart, Douglas A.; Cheng, Tina; Lupichuk, Sasha M.; Nodwell, Michael J.; Russell, James A.; Auer, Iwona A.; Morris, Donald G. [Reprint Author]
CORPORATE SOURCE: Department of Medicine, Tom Baker Cancer Centre, 1331 29 St NW, Calgary, AB, T2N 4N2, Canada
donmorri@cancerboard.ab.ca
SOURCE: Blood, (July 1 2003) Vol. 102, No. 1, pp. 377-387. print.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003

AB Hematologic stem cell rescue after high-dose cytotoxic therapy is extensively used for the treatment of many hematopoietic and solid cancers. Gene marking studies suggest that occult tumor cells within the autograft may contribute to clinical relapse. To date purging of

autografts contaminated with cancer cells has been unsuccessful. The selective oncolytic property of **reovirus** against myriad malignant histologies in in Vitro, in vivo, and ex vivo systems has been previously demonstrated. In the present study we have shown that **reovirus** can successfully purge cancer cells within autografts. Human monocytic and myeloma cell lines as well as enriched ex vivo lymphoma, myeloma, and Waldenstrom macroglobulinemia patient tumor specimens were used in in experimental purging model. Viability of the cell lines or purified ex vivo tumor cells of diffuse, large B-cell lymphoma, chronic lymphocytic leukemia, Waldenstrom macroglobulinemia, and small lymphocytic lymphoma was significantly reduced after **reovirus** treatment. Further, (35S)-methionine labeling and sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) of cellular proteins demonstrated **reovirus** protein synthesis and disruption of host cell protein synthesis as early as 24 hours. Admixtures of apheresis product with the above-mentioned tumor cells and cell lines treated with **reovirus** showed complete purging of disease. In contrast, **reovirus** purging of enriched ex vivo multiple myeloma, Burkitt lymphoma, and follicular lymphoma was incomplete. The oncolytic action of **reovirus** did not affect CD34+ stem cells or their long-term colony-forming assays even after granulocyte colony-stimulating factor (G-CSF) stimulation. Our results indicate the ex vivo use of an unattenuated oncolytic virus as an attractive purging strategy for autologous stem cell transplantations.

L15 ANSWER 15 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:323821 BIOSIS
DOCUMENT NUMBER: PREV200300323821
TITLE: **Reovirus** prolongs survival and reduces the frequency of spinal and leptomeningeal metastases from medulloblastoma.
AUTHOR(S): Yang, Wen Qing; Senger, Donna; Muzik, Huong; Shi, Zhong Qiao; Johnson, Denise; Brasher, Penny M. A.; Rewcastle, N. Barry; Hamilton, Mark; Rutka, Jim; Wolff, Johannes; Wetmore, Cynthia; Curran, Tom; Lee, Patrick W. K.; Forsyth, Peter A. [Reprint Author]
CORPORATE SOURCE: Department of Medicine, Tom Baker Cancer Centre, 1331 29 Street Northwest, Calgary, Alberta, T2N 4N2, Canada peter.forsyth@cancerboard.ab.ca
SOURCE: Cancer Research, (June 15 2003) Vol. 63, No. 12, pp. 3162-3172. print.
ISSN: 0008-5472 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jul 2003
Last Updated on STN: 16 Jul 2003

AB Medulloblastoma (MB), the most common pediatric brain tumor, is a highly malignant disease with a 5-year survival rate of only 60%. Tumor cells invade surrounding tissue and disseminate through cerebral spinal fluid, making treatment difficult. Human **reovirus** type 3 exploits an activated Ras pathway in tumor cells to support productive infection as an oncolytic virus. Here, we examined the ability of human **reovirus** to kill MB cells lines and surgical specimens in vitro and inhibit tumor growth/metastases in vivo. Most human MB cell lines tested (five of seven = 71.4%), two MB cell lines derived from spontaneously arising tumors in Patched-1+/- mice (two of two = 100%) and three MB primary cultures derived from surgical specimens, were susceptible to **reovirus** infection. **Reovirus** was internalized and transcribed in both susceptible and resistant cell lines. However, viral protein synthesis was restricted to cell lines with higher levels of activated Ras, suggesting that Ras plays a critical role in **reovirus oncolysis** in MB. Using an in vivo Daoy orthotopic animal model, we found that a single i.t. injection of **reovirus** dramatically prolonged survival compared with controls (160 versus 70 days, respectively; P = 0.0003). Repeating this experiment with GFP-labeled

Daoy cells and multiple i.t. administrations of **reovirus**, we again found prolonged survival and a dramatic reduction in spinal and leptomeningeal metastases (66.7% in control injections versus 0.0% in the live virus group). These data suggest that this oncolytic virus may be a potentially effective novel therapy against human MB. Its ability to reduce metastases to the spinal cord could allow a reduction in the dose/field of total neuroaxis cerebral-spinal radiotherapy currently used to treat/prevent cerebral spinal fluid dissemination.

L15 ANSWER 16 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:291259 BIOSIS
DOCUMENT NUMBER: PREV200300291259
TITLE: Selective **reovirus** killing of bladder cancer in a co-culture spheroid model.
AUTHOR(S): Kilani, Ruhangiz T.; Tamimi, Yahya; Hanel, Erich G.; Wong, Kevin K.; Karmali, Shahzeer; Lee, Patrick W. K.; Moore, Ronald B. [Reprint Author]
CORPORATE SOURCE: Department of Surgery, University of Alberta, 2D2.17 Walter Mackenzie Health Sciences Center, Edmonton, AB, T6G 2R7, Canada
ronald.moore@cancerboard.ab.ca
SOURCE: Virus Research, (May 2003) Vol. 93, No. 1, pp. 1-12. print.
CODEN: VIREDF. ISSN: 0168-1702.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jun 2003
Last Updated on STN: 19 Jun 2003

AB Up to 50% of the transitional cell carcinomas (TCC) express an activated EGF pathway involving MAP/MEK and RAF kinase thus providing a novel means to selectively eliminate transformed cells expressing such proteins. This EGF pathway expression phenotype was also confirmed in our MGH-U3 and room temperature-112 human TCC cell lines, which makes them a suitable model target for the **reovirus oncolysis**. We report here on an in vitro assay of co-culture spheroids using either human or rat TCC cells with their corresponding fibroblasts to examine the potential of viral selective lysis for TCC. **Reovirus**, a respiratory enteric orphan virus, which mammals are exposed to early in life, was used in this study. Selective killing of transformed versus normal cells was assayed by time-lapse photography, vital dye staining, immunohistochemistry, and MTT assay. In this in vitro bladder cancer model, **reovirus** selectively destroyed the transformed cells by lysis or induction of apoptosis. Based on these findings we have initiated an in vivo pre-clinical study on intravesical administration of **reovirus** in an animal model to further explore the effect of **reovirus** -mediated **oncolysis** of TCC.

L15 ANSWER 17 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:128450 BIOSIS
DOCUMENT NUMBER: PREV200300128450
TITLE: Oncolytic viruses for the therapy of brain tumors and other solid malignancies: a review.
AUTHOR(S): Fulci, Giulia [Reprint Author]; Chiocca, Ennio Antonio
CORPORATE SOURCE: Molecular Neuro-Oncology Laboratories, Massachusetts General Hospital, 13th Street, East Building, CNY6, Charlestown, MA, 02129, USA
gfulci@partners.org; chiocca@helix.mgh.harvard.edu
SOURCE: Frontiers in Bioscience, (May 1 2003) Vol. 8, No. Cited January 31, 2003, pp. e346-e360.
http://www.bioscience.org/. online.
ISSN: 1093-4715 (ISSN online).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 2003
Last Updated on STN: 5 Mar 2003

AB In spite of significant advances in the understanding of molecular processes in tumor biology that have led to the development of oncologic therapeutic strategies, the prognosis for several types of tumors (such as brain, pancreas, or hepatic malignancies) remains dismal. Without question, a strong need exists for continued investigations in new agents and new therapeutic regimens. The realization that several genes used by viruses in their lytic life cycle interact and/or complement the function of genes employed by cells in cellular events linked to cell cycle progression, apoptosis, and/or metabolism immediately suggests the development of treatment strategies wherein viral mutants could be employed as selective anticancer agents. Such viruses (designated as oncolytic viruses) can selectively grow in tumor cells, produce viral progeny in those cells, lyse them and release this progeny that can then infect additional cells in the tumor mass. A theoretical advantage of oncolytic viruses (OV) is that their numbers should augment within the tumor mass, a property that is lacking with drugs or radiation treatments. Additionally, Ovs' mode of tumor killing differs from standard anticancer agents, providing the possibility for synergistic interactions in multimodal tumor therapies. In this review, we will describe the development of OVs and briefly review the life cycle of their wild-type (wt) counterparts. We will also summarize published results from OV clinical trials and attempt to provide a perspective on research in this area.

L15 ANSWER 18 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:99636 BIOSIS
DOCUMENT NUMBER: PREV200300099636
TITLE: Novel approaches to cancer therapy using oncolytic viruses.
AUTHOR(S): Stanziale, S. F.; Fong, Y. [Reprint Author]
CORPORATE SOURCE: Department of Surgery, Hepatobiliary Division, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY, 10021, USA
fongy@mskcc.org
SOURCE: Current Molecular Medicine (Hilversum), (February 2003) Vol. 3, No. 1, pp. 61-71. print.
ISSN: 1566-5240 (ISSN print).
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2003
Last Updated on STN: 12 Feb 2003

L15 ANSWER 19 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:395709 BIOSIS
DOCUMENT NUMBER: PREV200200395709
TITLE: The molecular basis of Ras-dependent **reovirus oncolysis**.
AUTHOR(S): Norman, Kara L. [Reprint author]; Yang, An-Dao [Reprint author]; Hirasawa, Kensuke [Reprint author]; Lee, Patrick W. K. [Reprint author]
CORPORATE SOURCE: University of Calgary, Calgary, AB, Canada
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 664. print.
Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jul 2002
Last Updated on STN: 24 Jul 2002

L15 ANSWER 20 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:241645 BIOSIS

DOCUMENT NUMBER: PREV200200241645
TITLE: **Reovirus oncolysis** of human breast cancer.
AUTHOR(S): Norman, Kara L.; Coffey, Matthew C.; Hirasawa, Kensuke; Demetrick, Douglas J.; Nishikawa, Sandra G.; DiFrancesco, Lisa M.; Strong, James E.; Lee, Patrick W. K. [Reprint author]
CORPORATE SOURCE: Department of Microbiology and Infectious Diseases, University of Calgary Health Sciences Centre, Room B855, Calgary, AB, T2N 4N1, Canada
plee@ucalgary.ca
SOURCE: Human Gene Therapy, (March 20, 2002) Vol. 13, No. 5, pp. 641-652. print.
ISSN: 1043-0342.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Apr 2002
Last Updated on STN: 17 Apr 2002

AB We have previously shown that human **reovirus** replication is restricted to cells with an activated Ras pathway, and that **reovirus** could be used as an effective oncolytic agent against human glioblastoma xenografts. This study examines in more detail the feasibility of **reovirus** as a therapeutic for breast cancer, a subset of cancer in which direct activating mutations in the ras proto-oncogene are rare, and yet where unregulated stimulation of Ras signaling pathways is important in the pathogenesis of the disease. We demonstrate herein the efficient lysis of breast tumor-derived cell lines by the virus, whereas normal breast cells resist infection in vitro. In vivo studies of **reovirus** breast cancer therapy reveal that viral administration could cause tumor regression in an MDA-MB-435S mammary fat pad model in severe combined immunodeficient mice. **Reovirus** could also effect regression of tumors remote from the injection site in an MDA-MB-468 bilateral tumor model, raising the possibility of systemic therapy of breast cancer by the oncolytic agent. Finally, the ability of **reovirus** to act against primary breast tumor samples not propagated as cell lines was evaluated; we found that **reovirus** could indeed replicate in ex vivo surgical specimens. Overall, **reovirus** shows promise as a potential breast cancer therapeutic.

L15 ANSWER 21 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:570025 BIOSIS
DOCUMENT NUMBER: PREV200100570025
TITLE: Bioengineering the oncolytic potential of **reovirus** .
AUTHOR(S): Brown, Earl G. [Reprint author]; Liu, Hong [Reprint author]; Mbisa, Jean L. [Reprint author]; Bell, John [Reprint author]; Stojdl, David [Reprint author]
CORPORATE SOURCE: Centre for Research in Biopharmaceuticals and Dept. of Biochemistry, Microbiology and Immunology, University of Ottawa, Ottawa, Ontario, K1H 8M5, Canada
SOURCE: Gene Therapy, (October, 2001) Vol. 8, No. Supplement 1, pp. S7. print.
Meeting Info.: Harold W. Siebens Conference on Replicating Vectors for Gene Therapy. Rochester, Minnesota, USA. October 05-07, 2001.
ISSN: 0969-7128.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2001
Last Updated on STN: 25 Feb 2002

L15 ANSWER 22 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:359952 BIOSIS
DOCUMENT NUMBER: PREV200100359952

TITLE: Oncolytic viruses and cancer therapy.
AUTHOR(S): Norman, Kara L.; Farassati, Faris; Lee, Patrick W. K. [Reprint author]
CORPORATE SOURCE: Cancer Biology Research Group and Department of Microbiology and Infectious Diseases, University of Calgary, 3330 Hospital Drive N.W., Room B855, Health Sciences Building, Calgary, AB, T2N 4N1, Canada plee@ucalgary.ca
SOURCE: Cytokine and Growth Factor Reviews, (June-September, 2001) Vol. 12, No. 2-3, pp. 271-282. print. ISSN: 1359-6101.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 2001
Last Updated on STN: 19 Feb 2002

L15 ANSWER 23 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:333062 BIOSIS
DOCUMENT NUMBER: PREV200100333062
TITLE: **Reovirus** as an oncolytic agent against experimental human malignant gliomas.
AUTHOR(S): Wilcox, M. Elizabeth; Yang, WenQing; Senger, Donna; Rewcastle, N. Barry; Morris, Donald G.; Brasher, Penny M. A.; Shi, Z. Qiao; Johnston, Randal N.; Nishikawa, Sandi; Lee, P. W. K.; Forsyth, Peter A. [Reprint author]
CORPORATE SOURCE: Department of Oncology, Tom Baker Cancer Centre, 1331 29 St., N.W., Calgary, AB, T2N 4N2, Canada peter.forsyth@cancerboard.ab.ca
SOURCE: Journal of the National Cancer Institute (Bethesda), (June 20, 2001) Vol. 93, No. 12, pp. 903-912. print. CODEN: JNCIEQ. ISSN: 0027-8874.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2001
Last Updated on STN: 19 Feb 2002

AB Background: **Reovirus** is a naturally occurring oncolytic virus that usurps activated Ras-signaling pathways of tumor cells for its replication. Ras pathways are activated in most malignant gliomas via upstream signaling by receptor tyrosine kinases. The purpose of this study was to determine the effectiveness of **reovirus** as an experimental treatment for malignant gliomas. Methods: We investigated whether **reovirus** would infect and lyse human glioma cell lines in vitro. We also tested the effect of injecting live **reovirus** in vivo on human gliomas grown subcutaneously or orthotopically (i.e., intracerebrally) in mice. Finally, **reovirus** was tested ex vivo against low-passage cell lines derived from human glioma specimens. All P values were two-sided. Results: **Reovirus** killed 20 (83%) of 24 established malignant glioma cell lines tested. It caused a dramatic and often complete tumor regression in vivo in two subcutaneous (P=.0002 for both U251N and U87) and in two intracerebral (P=.0004 for U251N and P=.0009 for U87) human malignant glioma mouse models. As expected, serious toxic effects were found in these severely immunocompromised hosts. In a less immunocompromised mouse model, a single intratumoral inoculation of live **reovirus** led to a dramatic prolongation of survival (compared with control mice treated with dead virus; log-rank test, P<.0001 for both U251N and U87 cell lines). The animals treated with live virus also appeared to be healthier and gained body weight (P=.0001). We then tested the ability of **reovirus** to infect and kill primary cultures of brain tumors removed from patients and found that it killed nine (100%) of nine glioma specimens but none of the cultured meningiomas. Conclusions: **Reovirus** has potent activity against human malignant gliomas in vitro, in vivo, and ex vivo. **Oncolysis** with **reovirus** may be a potentially useful treatment for a broad range of human cancers.

L15 ANSWER 24 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:333060 BIOSIS
DOCUMENT NUMBER: PREV200100333060
TITLE: Viruses as therapeutic agents against malignant disease of the central nervous system.
AUTHOR(S): Gromeier, Matthias [Reprint author]
CORPORATE SOURCE: Department of Microbiology, Duke University Medical Center, Durham, NC, 27710, USA
grome001@mc.duke.edu
SOURCE: Journal of the National Cancer Institute (Bethesda), (June 20, 2001) Vol. 93, No. 12, pp. 889-890. print.
CODEN: JNCIEQ. ISSN: 0027-8874.
DOCUMENT TYPE: Article
Editorial
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2001
Last Updated on STN: 19 Feb 2002

L15 ANSWER 25 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:333331 BIOSIS
DOCUMENT NUMBER: PREV200000333331
TITLE: **Reovirus** as a novel oncolytic agent.
AUTHOR(S): Norman, Kara L.; Lee, Patrick W. K. [Reprint author]
CORPORATE SOURCE: Department of Microbiology and Infectious Diseases, University of Calgary, 3330 Hospital Drive NW, Room B855, Health Sciences Building, Calgary, AB, T2N 2N1, Canada
SOURCE: Journal of Clinical Investigation, (April, 2000) Vol. 105, No. 8, pp. 1035-1038. print.
CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Aug 2000
Last Updated on STN: 7 Jan 2002

L15 ANSWER 26 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:242127 BIOSIS
DOCUMENT NUMBER: PREV199900242127
TITLE: **Oncolysis** and tumor regression with **reovirus** in a malignant glioma model.
AUTHOR(S): Wilcox, M. Elizabeth [Reprint author]; Coffey, Matthew [Reprint author]; Strong, James [Reprint author]; Shi, Qiao [Reprint author]; Rewcastle, N. Barry [Reprint author]; Brasher, Penny M. [Reprint author]; Lee, Patrick W. K.; Forsyth, Peter
CORPORATE SOURCE: Univ. Calgary, Tom Baker Cancer Cent., Calgary, Alberta, Canada
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 421. print.
Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research. Philadelphia, Pennsylvania, USA. April 10-14, 1999. American Association for Cancer Research.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jun 1999
Last Updated on STN: 17 Jun 1999

L15 ANSWER 27 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:342077 BIOSIS
DOCUMENT NUMBER: PREV199800342077
TITLE: The molecular basis of viral **oncolysis**: Usurpation of the Ras signaling pathway by **reovirus**

AUTHOR(S): Strong, James E.; Coffey, Matthew C.; Tang, Damu; Sabinin, Pauline; Lee, Patrick W. K. [Reprint author]
CORPORATE SOURCE: Dep. Microbiol. Infect. Dis., Univ. Calgary Health Sci. Centre, Calgary, AB T2N 4N1, Canada
SOURCE: EMBO (European Molecular Biology Organization) Journal, (June 15, 1998) Vol. 17, No. 12, pp. 3351-3362. print. CODEN: EMJODG. ISSN: 0261-4189.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 1998
Last Updated on STN: 13 Aug 1998

AB NIH-3T3 cells, which are resistant to **reovirus** infection, became susceptible when transformed with activated Sos or Ras. Restriction of **reovirus** proliferation in untransformed NIH-3T3 cells was not at the level of viral gene transcription, but rather at the level of viral protein synthesis. An analysis of cell lysates revealed that a 65 kDa protein was phosphorylated in untransformed NIH-3T3 cells, but only after infection with **reovirus**. This protein was not phosphorylated in infected or uninfected transformed cells. The 65 kDa protein was determined to be the double-stranded RNA-activated protein kinase (PKR), whose phosphorylation leads to translation inhibition. Inhibition of PKR phosphorylation by 2-aminopurine, or deletion of the Pkr gene, led to drastic enhancement of **reovirus** protein synthesis in untransformed cells. The emerging picture is one in which early viral transcripts trigger PKR phosphorylation in untransformed cells, which in turn leads to inhibition of translation of viral genes; this phosphorylation event is blocked by an element(s) in the Ras pathway in the transformed cells, allowing viral protein synthesis to ensue. The usurpation of the Ras signaling pathway therefore constitutes the basis of **reovirus oncolysis**.

L15 ANSWER 28 OF 32 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1979:91560 BIOSIS
DOCUMENT NUMBER: PREV197917031560; BR17:31560
TITLE: CHARACTERISTICS OF **REOVIRUS** INFECTION OF L-1210 CELLS.
AUTHOR(S): COX D C; STANISH S M; KOLLMORGEN G M
SOURCE: Abstracts of the Annual Meeting of the American Society for Microbiology, (1979) No. 79, pp. 263. CODEN: ASMACK. ISSN: 0094-8519.
DOCUMENT TYPE: Article
FILE SEGMENT: BR
LANGUAGE: Unavailable

L15 ANSWER 29 OF 32 CANCERLIT on STN
ACCESSION NUMBER: 2002155979 CANCERLIT
DOCUMENT NUMBER: 21914443 PubMed ID: 11916487
TITLE: **Reovirus oncolysis** of human breast cancer.
AUTHOR: Norman Kara L; Coffey Matthew C; Hirasawa Kensuke; Demetrick Douglas J; Nishikawa Sandra G; DiFrancesco Lisa M; Strong James E; Lee Patrick W K
CORPORATE SOURCE: Cancer Biology Research Group, Faculty of Medicine, University of Calgary, Calgary, Alberta, T2N 4N1 Canada.
SOURCE: HUMAN GENE THERAPY, (2002 Mar 20) 13 (5) 641-52. Journal code: 9008950. ISSN: 1043-0342.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 2002184133
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020726
Last Updated on STN: 20020726

AB We have previously shown that human **reovirus** replication is restricted to cells with an activated Ras pathway, and that **reovirus** could be used as an effective oncolytic agent against human glioblastoma xenografts. This study examines in more detail the feasibility of **reovirus** as a therapeutic for breast cancer, a subset of cancer in which direct activating mutations in the ras proto-oncogene are rare, and yet where unregulated stimulation of Ras signaling pathways is important in the pathogenesis of the disease. We demonstrate herein the efficient lysis of breast tumor-derived cell lines by the virus, whereas normal breast cells resist infection in vitro. In vivo studies of **reovirus** breast cancer therapy reveal that viral administration could cause tumor regression in an MDA-MB-435S mammary fat pad model in severe combined immunodeficient mice. **Reovirus** could also effect regression of tumors remote from the injection site in an MDA-MB-468 bilateral tumor model, raising the possibility of systemic therapy of breast cancer by the oncolytic agent. Finally, the ability of **reovirus** to act against primary breast tumor samples not propagated as cell lines was evaluated; we found that **reovirus** could indeed replicate in ex vivo surgical specimens. Overall, **reovirus** shows promise as a potential breast cancer therapeutic.

L15 ANSWER 30 OF 32 CANCERLIT on STN
ACCESSION NUMBER: 2002151008 CANCERLIT
DOCUMENT NUMBER: 21959494 PubMed ID: 11961194
TITLE: Viral **oncolysis**.
AUTHOR: Mullen John T; Tanabe Kenneth K
CORPORATE SOURCE: Division of Surgical Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02114-2696, USA.
SOURCE: ONCOLOGIST, (2002) 7 (2) 106-19. Ref: 90
Journal code: 9607837. ISSN: 1083-7159.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 2002225354
ENTRY MONTH: 200206
ENTRY DATE: Entered STN: 20020726
Last Updated on STN: 20020726

AB The concept of using replicating viruses as anticancer agents is not a new one, but the ability to genetically modify these viruses into increasingly potent and tumor-specific vectors is a recent phenomenon. As more is learned about the functions of viral gene products in controlling the mammalian cell cycle and in disabling cellular defense mechanisms, specific viral functions can be augmented or eliminated to enhance antineoplastic efficacy. In this article, general mechanisms by which oncolytic viruses achieve their antitumor efficacy and specificity are reviewed. The paradoxical roles of the immune response are addressed with respect to oncolytic viral therapy, as it, on one hand, impedes the spread of viral infection, and on the other, augments tumor cell destruction through the recruitment of T cells "vaccinated" against tumor antigens. The most commonly used oncolytic viruses are each reviewed in turn, including adenoviruses, herpes simplex viruses, vaccinia viruses, **reoviruses**, and Newcastle disease viruses. Special attention is focused on the unique biology of each of these viruses as well as the status of several of these mutants in clinical trials.

L15 ANSWER 31 OF 32 CANCERLIT on STN
ACCESSION NUMBER: 2002061672 CANCERLIT
DOCUMENT NUMBER: 21309242 PubMed ID: 11416111
TITLE: **Reovirus** as an oncolytic agent against experimental human malignant gliomas.
COMMENT: Comment in: J Natl Cancer Inst. 2001 Jun 20;93(12):889-90

L15 ANSWER 32 OF 32 CANCERLIT on STN
ACCESSION NUMBER: 1998292455 CANCERLIT
DOCUMENT NUMBER: 98292455 PubMed ID: 9628872
TITLE: The molecular basis of viral **oncolysis**: usurpation of the Ras signaling pathway by **reovirus**.
AUTHOR: Strong J E; Coffey M C; Tang D; Sabinin P; Lee P W
CORPORATE SOURCE: Department of Microbiology and Infectious Diseases, University of Calgary Health Sciences Centre, Calgary, Alberta, Canada T2N 4N1.
SOURCE: EMBO JOURNAL, (1998 Jun 15) 17 (12) 3351-62. Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 1998292455
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980910
Last Updated on STN: 19980910

AB NIH-3T3 cells, which are resistant to **reovirus** infection, became susceptible when transformed with activated Sos or Ras. Restriction of **reovirus** proliferation in untransformed NIH-3T3 cells was not at the level of viral gene transcription, but rather at the level of viral protein synthesis. An analysis of cell lysates revealed that a 65 kDa protein was phosphorylated in untransformed NIH-3T3 cells, but only after infection with **reovirus**. This protein was not phosphorylated in infected or uninfected transformed cells. The 65 kDa protein was determined to be the double-stranded RNA-activated protein kinase (PKR), whose phosphorylation leads to translation inhibition. Inhibition of PKR phosphorylation by 2-aminopurine, or deletion of the Pkr gene, led to drastic enhancement of **reovirus** protein synthesis in untransformed cells. The emerging picture is one in which early viral transcripts trigger PKR phosphorylation in untransformed cells, which in turn leads to inhibition of translation of viral genes; this phosphorylation event is blocked by an element(s) in the Ras pathway in the transformed cells, allowing viral protein synthesis to ensue. The usurpation of the Ras signaling pathway therefore constitutes the basis of **reovirus oncolysis**.

L40 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:394061 CAPLUS
DOCUMENT NUMBER: 138:384157
TITLE: Methods for preventing **reovirus** recognition for the treatment of cellular proliferative disorders
INVENTOR(S): Coffey, Matthew C.; Thompson, Bradley G.
PATENT ASSIGNEE(S): Oncolytics Biotech Inc., Can.
SOURCE: U.S., 14 pp., Cont.-in-part of U.S. 6,136,307.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6565831	B1	20030520	US 2000-636597	20000810
US 6136307	A	20001024	US 1999-256824	19990224
WO 2002011742	A3	20020418	WO 2001-CA1055	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1309334	A2	20030514	EP 2001-953727	20010720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001013128	A	20030722	BR 2001-13128	20010720
JP 2004505924	T2	20040226	JP 2002-517077	20010720
US 2003215443	A1	20031120	US 2003-401032	20030328

PRIORITY APPLN. INFO.:
US 1999-256824 A2 19990224
US 1997-911383 A2 19970813
US 2000-636597 A1 20000810
WO 2001-CA1055 W 20010720

AB The present invention pertains to methods for preventing **reovirus** recognition in the treatment of cellular proliferative disorders, and particularly ras-mediated cellular proliferative disorders, in mammals. The method comprises suppressing or otherwise inhibiting the immune system of the mammal and, concurrently or subsequently, administering to the proliferating cells an effective amount of one or more **reoviruses** under conditions which result in substantial lysis of the proliferating cells. The methods may include the selective removal of immune constituents that may interfere with the systemic delivery of the virus; preventing **reovirus** recognition by the host immune system; and removal of the virus from an immune suppressed or immune incompetent host following treatment with **reovirus**. Alternatively, **reovirus** may be administered to a mammal with a diminished immune response system under conditions which result in substantial lysis of the proliferating cells.

L40 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:636057 CAPLUS
DOCUMENT NUMBER: 125:316583
TITLE: Inhibition of **reovirus**-stimulated murine natural killer cell cytotoxicity by cyclosporine
AUTHOR(S): Al-Sheboul, Suhaila; Crosley, Dianne; Steele, Timothy A.
CORPORATE SOURCE: Dep. of Health Sciences, Univ. of Wisconsin-Milwaukee, Milwaukee, WI, 53201, USA
SOURCE: Life Sciences (1996), 59(20), 1675-1682
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Reovirus** type 3 is a double-stranded RNA virus that is a potent inducer of murine natural killer (NK) cell cytotoxicity, most likely as a result of virus-induced interferon production We determined that **reovirus** was an effective inducer of high levels of NK cytotoxicity. A single injection of cyclosporine (CS), administered concurrently with **reovirus** or delayed until three days after injecting CS, significantly inhibited NK cytotoxicity. CS significantly suppressed **reovirus**-induced NK cytotoxicity when added directly to the chromium-release assay. We determined that CS inhibited the ability of murine spleen cells to form conjugates with YAC-1 tumor target cells. Finally, CS was shown to directly inhibit **reovirus** replication in vitro. Our results demonstrate that CS is an effective inhibitor of **reovirus**-induced NK cytotoxicity and suggest that inhibition occurs through multiple mechanisms including direct effects on the NK cells and direct inhibition of virus replication.

L3 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:460708 BIOSIS
DOCUMENT NUMBER: PREV200100460708
TITLE: **Reovirus** therapy of metastatic cancer models in immune-competent mice.
AUTHOR(S): Hirasawa, Kensuke [Reprint author]; Yoon, Chang-Soon [Reprint author]; Nishikawa, Sandra G. [Reprint author]; Waisman, David M. [Reprint author]; Lee, Patrick W. K. [Reprint author]
CORPORATE SOURCE: University of Calgary, Calgary, AB, Canada
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 453. print.
Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 2001
Last Updated on STN: 22 Feb 2002

L17 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:20988 CAPLUS
DOCUMENT NUMBER: 140:73576
TITLE: Oncolytic viruses as phenotyping agents for neoplasms and use for tumor diagnosis and therapy
INVENTOR(S): Thompson, Bradley G.; Coffey, Matthew C.
PATENT ASSIGNEE(S): Oncolytics Biotech, Inc., Can.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004003562	A2	20040108	WO 2003-CA951	20030625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004029112	A1	20040212	US 2003-602024	20030624

PRIORITY APPLN. INFO.: US 2002-392031P P 20020628
US 2003-443188P P 20030129

AB The present invention provides a method of diagnosing neoplasms having a particular phenotype by using oncolytic viruses that selectively replicate in neoplasms having the particular phenotype. For example, **reovirus** does not replicate in normal cells. However, **reovirus** selectively replicate in cells with an activated ras pathway, which leads to death of these cells. Therefore, a cell which becomes neoplastic due to, at least in part, elevated ras pathway activities can be diagnosed by its susceptibility to **reovirus** replication. This invention can further be applied, using other oncolytic viruses, to the diagnosis and/or **treatment** of other tumors, such as **interferon**-sensitive tumors, p53-deficient tumors and Rb-deficient tumors. Kits useful in the diagnosis or **treatment** disclosed herein are also provided.

L17 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:241289 CAPLUS
DOCUMENT NUMBER: 136:257234
TITLE: Purging of cells using viruses
INVENTOR(S): Atkins, Harold L.; Bell, John C.; Heilman, Conrad J.; Lichty, Brian D.; Lorence, Robert M.; Roberts, Michael S.; Stojdl, David F.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002037543	A1	20020328	US 2001-888626	20010626
WO 2002000233	A2	20020103	WO 2001-US41121	20010626

WO 2002000233 A3 20020822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1297121 A2 20030402 EP 2001-957529 20010626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004501200 T2 20040115 JP 2002-505015 20010626
PRIORITY APPLN. INFO.: US 2000-214014P P 20000626
WO 2001-US41121 W 20010626

AB The subject invention relates to viruses that are able to purge (reduce or eliminate) undesirable cells in a mixture of cells. Undesirable cells can include neoplastic cells, cells mediating graft-vs. host diseases, and autoimmune cells. The subject invention also relates to the purging of undesirable cells from bone marrow or peripheral blood cell harvests in the **treatment** of mammals including **cancer** patients, transplant recipients, and patients with autoimmune disease. Vesicular stomatitis virus (VSV) Indiana serotype showed selective destruction of leukemic cells in a mixed population of normal marrow containing leukemic OCI/AML3 cells.

L25 ANSWER 4 OF 4 CANCERLIT on STN
ACCESSION NUMBER: 80677123 CANCERLIT
DOCUMENT NUMBER: 80677123
TITLE: APPLICATIONS OF RADIOIMMUNOASSAY IN THE STUDY OF VIRUSES AND ANTICANCER DRUGS.
AUTHOR: Toyoshima S
CORPORATE SOURCE: Div. Chemotherapy, Pharmaceutical Inst., Keio Univ., Sch. Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan.
SOURCE: Radioisotopes, (1980) 29 (5) 252-260.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: Japanese
FILE SEGMENT: Institute for Cell and Developmental Biology
ENTRY MONTH: 198010
ENTRY DATE: Entered STN: 19941107
Last Updated on STN: 19960517

AB The current applications of radioimmunoassay (RIA) for the quantitative study of viruses and anticancer drugs are reviewed. RIA is being used to study quiescent viral infections, **reoviruses**, the activity of interferon in virus-bearing hosts, the presence of interferon in cells, Type C viruses, protein matrices, and the LD50 of anticancer drugs on host cells and microorganisms. Anticancer drugs are studied with RIA based on the production of antibodies with the anticancer drugs acting as haptens. The haptens that were studied included melphalan, **methotrexate**, 1-(5-O-succinyl-beta-D-arabinofurasyl) cytosine (ara-C), NaIO4 acidified 5-fluorodeoxyuridine, adriamycin, bleomycin, N-deacetylthiocolchicine, and vinblastine. The studies were performed with hapten-associated antigens in Freund's complete adjuvant or Marcol 52/Arlacel(9.1)-BCGT-Tween 80 injected into rabbits, goats, or monkeys. The conditions of pH, temperature, and other variables influencing the radioimmunoassays of the various anticancer drugs are described. The limits of drug determination with RIA depended on the method of fractionation and ranged from 0.02-0.2 nanog/tube for ara-C to 1-100 nanog/tube for colchicine. (78 Refs)

L25 ANSWER 3 OF 4 CANCERLIT on STN
ACCESSION NUMBER: 85108122 CANCERLIT
DOCUMENT NUMBER: 85108122 PubMed ID: 3968718
TITLE: Cellular integrity is required for inhibition of initiation of cellular DNA synthesis by **reovirus** type 3.
AUTHOR: Roner M R; Cox D C
SOURCE: JOURNAL OF VIROLOGY, (1985 Feb) 53 (2) 350-9.
Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: MEDLINE; Priority Journals
OTHER SOURCE: MEDLINE 85108122
ENTRY MONTH: 198503
ENTRY DATE: Entered STN: 19990618
Last Updated on STN: 19990618

AB Synchronized HeLa cells, primed for entry into the synthesis phase by amethopterin, were prevented from initiating DNA synthesis 9 h after infection with **reovirus** type 3. However, nuclei isolated from synchronized cells infected with **reovirus** for 9 or 16 h demonstrated a restored ability to synthesize DNA. The addition of enucleated cytoplasmic extracts from infected or uninfected cells did not affect this restored capacity for synthesis. The addition of ribonucleotide triphosphates to nuclei isolated from infected cells stimulated additional DNA synthesis, suggesting that these nuclei were competent to initiate new rounds of DNA replication. Permeabilization of infected cells did not restore the ability of these cells to synthesize DNA. Nucleoids isolated from intact or permeabilized cells, infected for 9 or 16 h displayed an increased rate of sedimentation when compared with nucleoids isolated from uninfected cells. Nucleoids isolated from the nuclei of infected cells demonstrated a rate of sedimentation similar to that of nucleoids isolated from the nuclei of uninfected cells. The inhibition of initiation of cellular DNA synthesis by **reovirus** type 3 appears not to have been due to a permanent alteration of the replication complex, but this inhibition could be reversed by the removal of that complex from factors unique to the structural or metabolic integrity of the infected cell.

L36 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:657956 CAPLUS
DOCUMENT NUMBER: 137:179862
TITLE: Sensitization of chemotherapeutic agent resistant neoplastic cells with **reovirus**
INVENTOR(S): Coffey, Matthew C.; Thompson, Bradley G.
PATENT ASSIGNEE(S): Oncolytics Biotech Inc., Can.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066040	A2	20020829	WO 2002-CA201	20020219
WO 2002066040	C1	20030320		
WO 2002066040	A3	20030530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002168344	A1	20021114	US 2002-76074	20020215
EP 1361884	A2	20031119	EP 2002-701122	20020219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-270363P P 20010220
WO 2002-CA201 W 20020219

AB The present invention relates to a method of increasing the sensitivity of neoplastic cells to chemotherapeutic agents by using **reovirus**, a method of treating proliferative disorders with **reovirus** and chemotherapeutic agents, and a method for preventing a neoplasm from developing drug resistance to chemotherapeutic agents.